

PHOSPHOLIPID COMPOUNDS OF IMPORTANCE

Color index:

- **Important**
- Extra explanation

“OPPORTUNITIES DON’T HAPPEN,
YOU CREATE THEM.”

Recall

What are phospholipids?

A **phospholipid** are compounds composed of **2 fatty acid chains** (tails) attached to 2 carbons of a **glycerol** molecule, and **phosphate group** attached to the third carbon of glycerol.

They are divided into : 1- hydrophilic head (glycerol & phosphate).

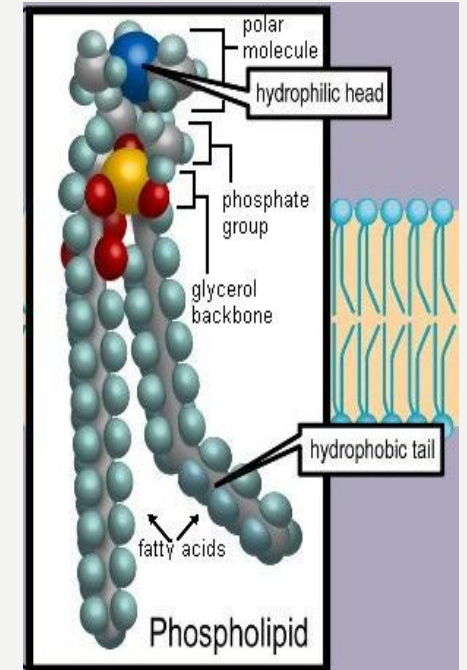
2-hydrophobic tails (fatty acids chains.)

Thus, it is amphipathic (contain both hydrophobic & hydrophilic characters).

What are triacylglycerols?

A **triacylglycerol** is a compound composed of **glycerol** molecule plus **3 fatty acids** (the same structure of phospholipids but with a third fatty acid chain instead of phosphate).

- it's the storage form in adipose tissue.



Triacylglycerols is transported in blood by :

chylomicrons & very low density lipoproteins (VLDL).

Cholesterol transportation in blood:

Free cholesterol: by low density lipoproteins (LDL)

Esterified cholesterol : by high density lipoproteins (HDL)

OBJECTIVES

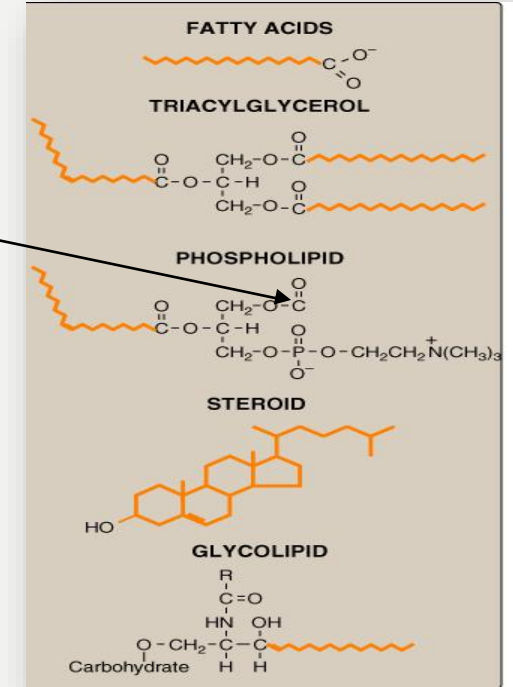
- ✓ Discuss selected members of phospholipids
- ✓ Describe the physiological importance of phospholipids with specific examples
- ✓ Distinguish various Phospholipases and describe their roles:
 - Phospholipases A1, A2, C and D
 - Lysosomal phospholipase: Sphingomyelinase
- ✓ To understand the diseases associated with globular proteins.

Lipids

LIPID COMPOUNDS CHARACTERS:

- 1- Heterogeneous group.
- 2- water-insoluble **except the ketone bodies.**
- 3- Soluble in non-polar solvents.

Note:
 الدكتور عمرو ذكر إن فيه خطأ هنا
 وأن المفروض يكون فيه فاتي
 اسيد ثاني على هذه الكربونة.



Classes of lipids compounds



Phospholipids

CLASSIFICATIONS OF PHOSPHOLIPIDS:

Glycerophospholipids

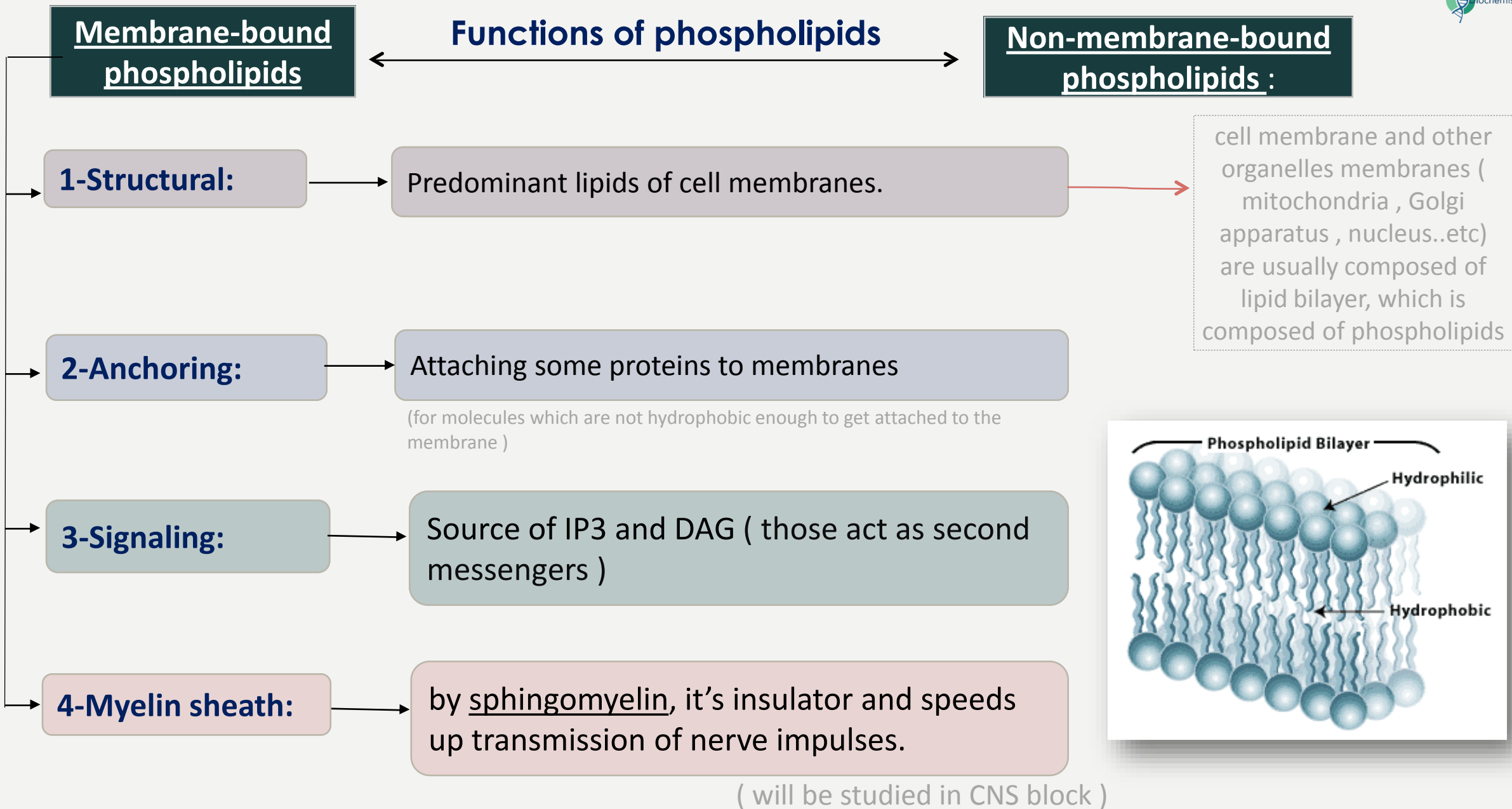
- They're **Glycerol** (alcohol)-containing phospholipids.
- they're Degraded and remodeled by: phospholipases.

Degradation and remodeling

Sphingophospholipids

- **Sphingosine** (amino alcohol)-containing phospholipids.
- They're Present in myelin sheath.
- They're Degraded by: lysosomal phospholipases (sphingomyelinases).

Degradation only



Functions of phospholipids

Membrane-bound phospholipids

Non-membrane-bound phospholipids :

Bile is secreted from liver & stored in gall bladder. It's function : helping in digestion of lipids.

Essential component of bile

- Gallstones may develop when there is too much cholesterol in the bile secreted by your liver. Bile usually dissolves or breaks down cholesterol. However, if your liver makes more cholesterol than your bile can dissolve, hard stones may develop.

-Solubilize cholesterol. Thus, preventing gall stones.

-Emulsifying lipids to help in lipid digestion.

Emulsification:

Fat is hydrophobic compound, but it's surface is hydrophilic. When we eat fat, it must be small enough to get digested properly. If there was a deficiency of phospholipids in bile, the digestive enzymes will act on the surface only (because the fat molecule is large).

1- Easy re-inflation of alveoli by air: Lung surfactant.

2- Detergent effect: :

Detergent:

مثل مساحيق الغسيل عندما تقوم بتدوير البقع الدهنية ، فهذا يساعد على تدوير الليبوز من أجل أهداف معينة.

2-Structural: :
Coat of lipoproteins.

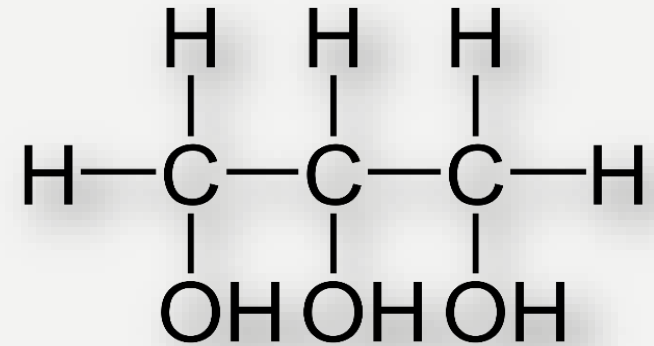
Glycerophospholipids

PARENT COMPOUND : Phosphatidic acid

Extra:

This is a glycerol molecule

1. Mono-acylglycerol: if 1 fatty acid binds instead of OH
2. di-acylglycerol: if 2 fatty acids bind instead of 2 OH
3. phosphatidic acid: 2 fatty acid + Phosphate group
Instead of all three OH .



Parent compound :

يعني أنه هو المركب الأب الذي يجب أن يتوفر بجميع الجليسر وفوسفوليبيدز

Members of Glycerophospholipids “Family”:

- 1. Phosphatidylcholine (Lecithin).

e.g., **Surfactant (Dipalmitoylecithin)**

“Di” because of 2 palmitic acid (16 carbon fatty acid).

- **surfactant** is a special type of lecithin that reduces the surface tension preventing alveolar collapse.

- **Surfactant is composed of:** 65% **Dipalmitoylecithin** and 35% of other **phospholipids, cholesterol, and protein**

- 2. Phosphatidylinositol.

Signaling and anchoring molecule.

Note:

Dipalmitoylecithin

هو نفسه :

dipalmitoylphosphatidylcholine

الي درسناه في محاضرة الفيسيولوجي.

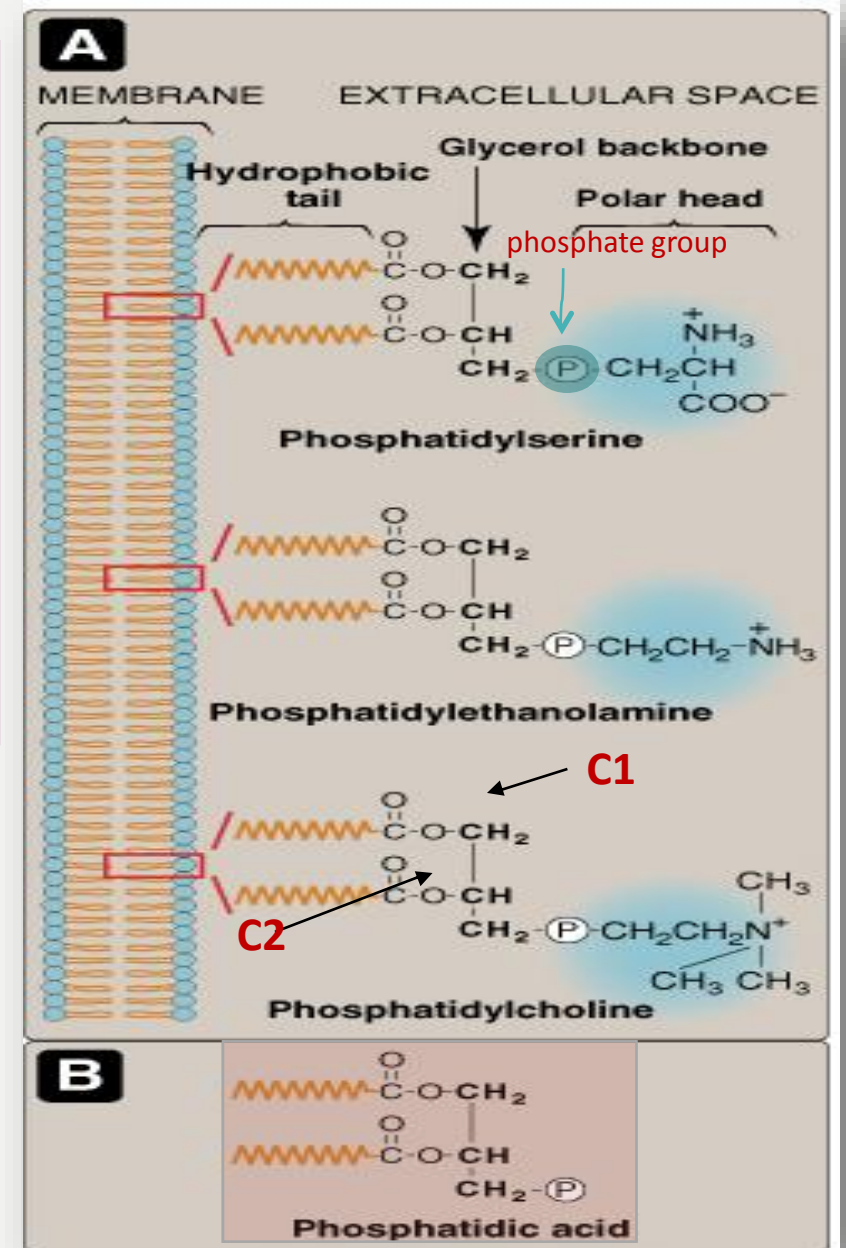
- we can get different **Glycerophospholipids** , by Adding some compounds to the phosphate group “of the phosphatidic acid”. examples:

- By adding serine → phosphatidylserine.
- By adding ethanolamine → phosphatidylethanolamine.
- By adding choline → Phosphatidylcholine.

- الدوائر الزرقاء في الصورة هي مركبات اذا ارتبطت بالفوسفات كونت مركب اخر يحمل اسمها (مثل كولين نضيفها للفوسفاتديك من جهة الفوسفات فيصبح المركب فوسفاتيديل كولين).

Notes:

- The fatty acid attached to C1 is always **saturated**, while the one which is attached to the C2 is usually **unsaturated**.
- Those two fatty acids will have **different** structures.



DIPALMITOYLECITHIN (LUNG SURFACTANT)

- What is it?

It is the **major** lipid component (**65%**) of lung surfactant (Remaining **35%**: Other **phospholipids**, **cholesterol** & **proteins**).

- Synthesized and secreted: **by granular pneumocytes**.
(type II, from the first lecture of physiology)

- Importance:

- Decreases surface tension of fluid layer lining of alveoli.
- Reduces the pressure needed for their inflation by air.
- Prevents **alveolar collapse (atelectasis)**.

- كيف نتذكر اسم المركب ؟
*نسال نفسنا كم عندي بالم (راحة يد) ؟ عندي ٢ بالمز

Di-palmi



*لمن كنتو صغار وش كنتو تمسكون فيه؟ توييز

Di-palmi-toy



- ثم نضيف اسم العائلة (لسثن)

Di-palmi-toy-lecithin

CONGENITAL RESPIRATORY DISTRESS SYNDROME (RDS):

- What is it?

It refers to **Insufficient production of lung surfactant**

- Where does it occur?

It occurs in **pre-term babies**. (babies born in the 32nd or the 33rd week).

- What does it cause?

It causes **neonatal death**



- Pre-natal diagnosis to RDS is done by:

Lecithin/sphingomyelin (L/S) ratio in amniotic fluid.

- If the ratio is **2** or above → indicates lung maturity and **no RDS**.
- To the **week 32** there are **sphingomyelin** in lungs, but by this week **it shift to lecithin** which means the lung is mature.

- Prevention:

By giving **Glucocorticoids** to the pregnant mother with low L/S ratio shortly before delivery (usually before several days).

- Treatment:

If the doctors couldn't prevent the RDS and the pre-term infant born with it, they can treat him by **Intra-tracheal administration of surfactant** to him.

RDS- EXTRA EXPLANATION

- هي عبارة عن متلازمة ، سببها الرئيسي هو نقص السرفاكتنت في الرئة.

- تحدث في الأطفال الذين يولدون قبل الأسبوع ال ٣٢ من الحمل ، لماذا؟

كما ذكرنا في السلايدات الماضية أن الـ Surfactant مكون من عدة أشياء ولكن نسبة كبيرة منه ٦٥% يتكون من Lecithin ، هذا الـ surfactant لا يتكون إلى عند الأسبوع ال ٣٢ ، وذلك عند تحول الـ Sphingomyelin إلى الـ Lecithin (المكون الرئيسي) .

- كيف يتم تشخيص هذه المتلازمة؟

يتم تشخيصها عن طريق حساب نسبة الـ Sphingomyelin إلى الـ Lecithin ، إذا كانت النسبة ٢ أو أكثر فهذا دليل على نضوج الرئة وأن الشخص لا يعاني من هذه المتلازمة.

- كيف يتم منع هذه المتلازمة ؟

عن طريق إعطاء الأم **Glucocorticoids** قبل الولادة.
(طبعا هنا في حالة التشخيص قبل الولادة ، عرفنا ونبي نمنع حصول المتلازمة)

- كيف يتم علاج المتلازمة، إذا لم يتم تشخيصها قبل الولادة؟

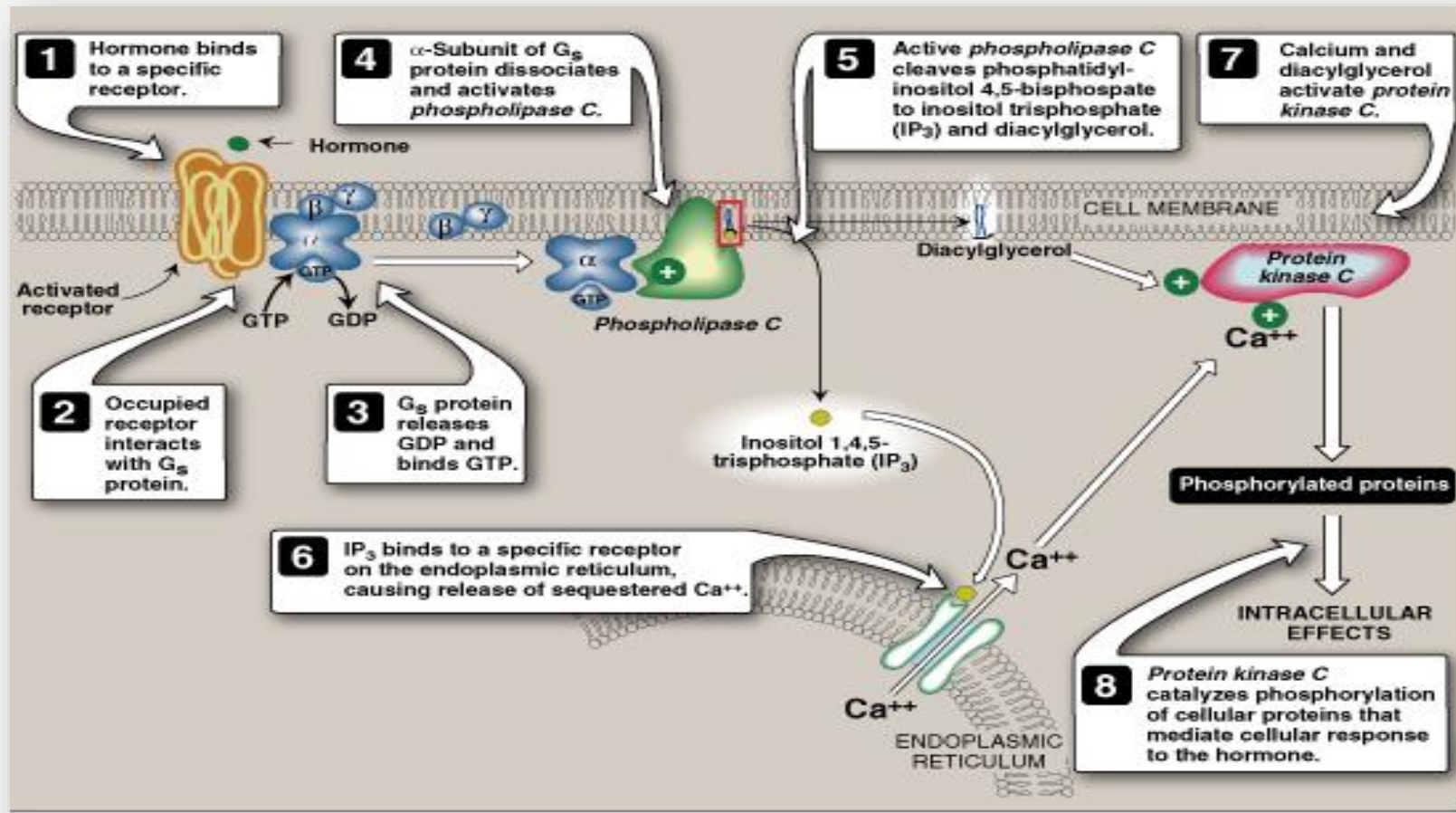
عن طريق إعطاء الطفل **Intra-tracheal administration of surfactant**

PHOSPHATIDYLINOSITOL SYSTEM



[Phosphatidylinositol system](#)

فيديو جميل مدته خمس دقائق يعطيك فكرة عن هذا النظام ، يفضل فتحه قبل اكمال السلايدز.

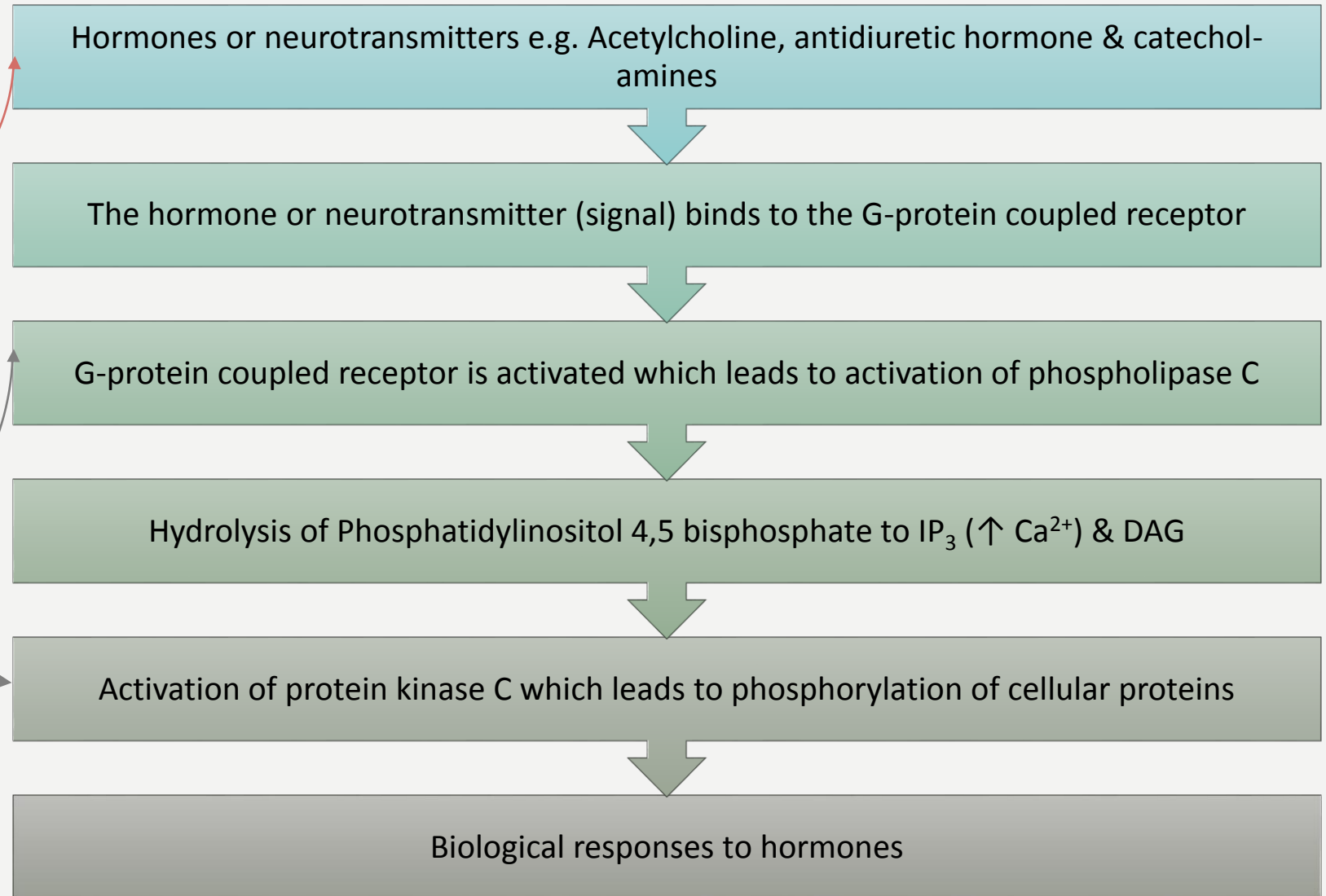


PHOSPHATIDYLINOSITOL SYSTEM

Notes:

- Acetylcholine & antidiuretic hormone bind to (V1-receptor)
- Catechol-amines bind to (α_1 receptor)
- antidiuretic hormone act on two kinds of receptors : v1 & v2 *Will be discussed in renal block*.

“C” in phospholipase C & protein Kinase C refers to “Calcium”.

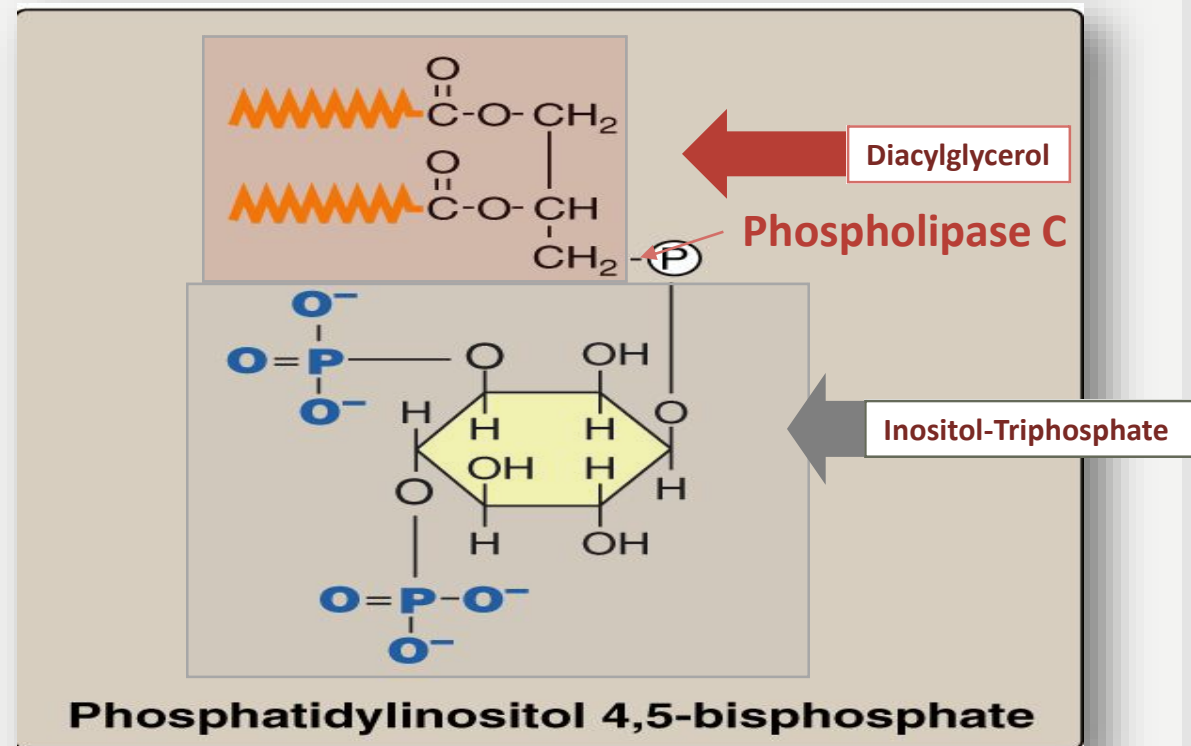


CALCIUM/PHOSPHATIDYLINOSITOL SYSTEM

phospholipase C
breaks the link

results in cleaving
(DAG)* & (IP₃)*

DAG & IP₃ acts as
second messenger



Phospholipase C comes and breaks “phosphatidylinositol 4,5-bisphosphate” into two compounds:

- 1- DAG = Diacylglycerol.
- 2- IP₃ = Inositol-Triphosphate.

CALCIUM/PHOSPHATIDYLIOSITOL SYSTEM

Phosphatidylinositol-Protein Anchoring:

- Another function of phosphatidylinositol is: protein anchoring. (in addition to the “signaling” function.)
- Anchoring of proteins to membranes is done via: Carbohydrate-phosphatidylinositol Bridge.
- Some enzymes can be **active** when they get attached to the membrane by phosphatidylinol , while other enzymes may be **inactive** when they get attached to the membrane (depending on the kind of enzyme).

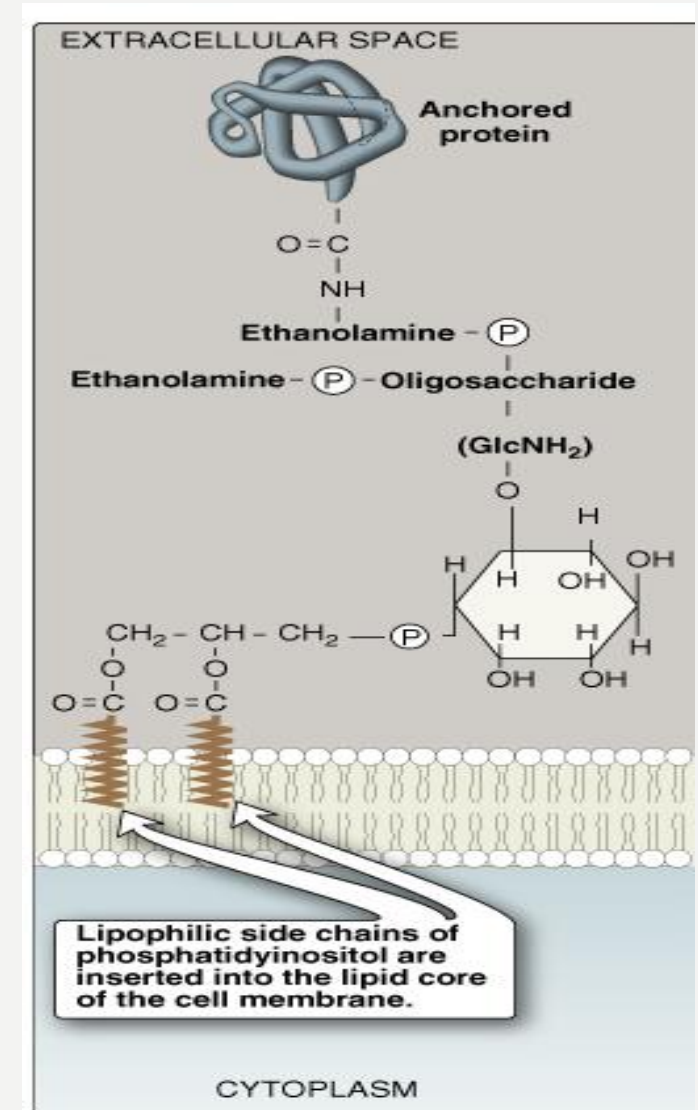
Examples of anchored proteins :-

Alkaline phosphatase

- Attached to the surface of small intestine

Acetylcholine esterase

- Attached to postsynaptic membrane.



Important: These proteins can be cleaved from their attachment to the membranes by **phospholipase C**

LIPOPROTEIN STRUCTURE

- **Lipoproteins** are the way of the lipids (which are hydrophobic) to get transported in the circulation (which is hydrophilic).

*الليبيدز تتركه الماء ولازم تمر بالسركليشين والتي هي للاسف محبة للماء، فلازم تدور لها على حل علسان تمر بدون مايصير فيه بينهم «حرب» ، والحل هو أن تلبس عباية «محبة للماء» علسان تقدر تمر بسلام وأمان بدون ماتحس عليها السركليشين، وأخذت إسم مستعار «لايبو بروتينز».

They have 2 parts:

The Outer part (surface coat)

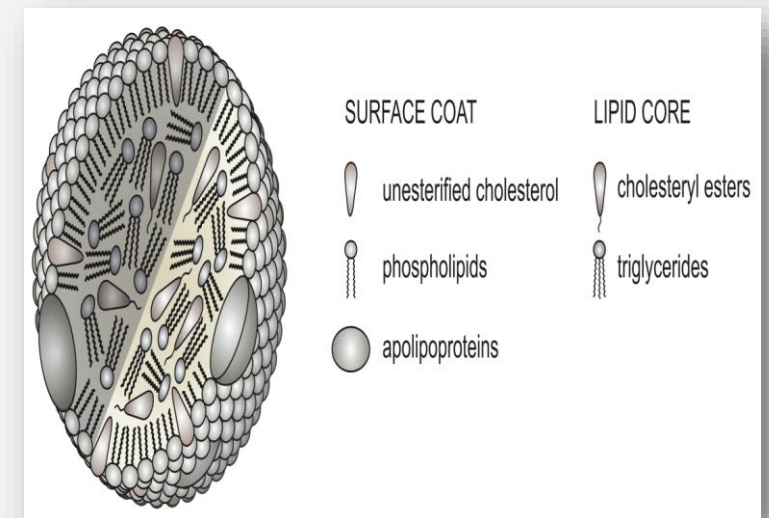
Consists of:

- Apo-proteins or apolipoproteins.
- Phospholipids. (Hydrophilic part will be in the outer surface, and the hydrophobic part will be in the inner surface)
- Free cholesterol (unesterified) .

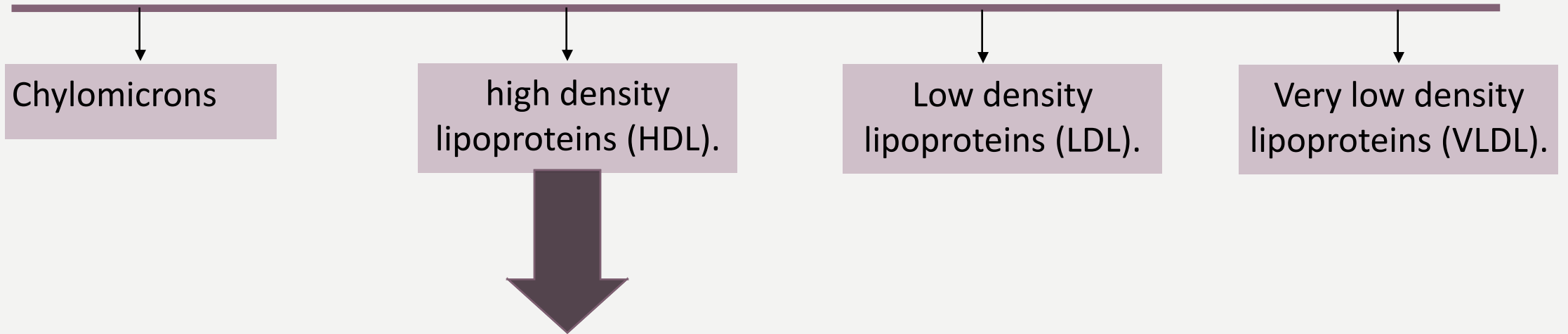
Inner part (lipid core)

- According to the type of lipoproteins. (it can be HDL, VLDL, LDL or chylomicron)
- Different lipid components in various combinations.

Note: The coat is Relatively hydrophilic, allowing transport of lipid particles of the core in the aqueous plasma)



CLASSES OF LIPOPROTEINS



- HDL has **the highest** content of Phospholipids. (very Important)
- **Phosphatidylcholine (lecithin) acts as:** a source for fatty acids necessary for esterification of cholesterol on the surface of HDL by lecithin-cholesterol acyl transferase (*LCAT/*PCAT).
- **The surface of HDL consists of :** phospholipids, cholesterol and LCAT.
- LCAT transfers acyl group from lecithin to the cholesterol of the HDL “by esterification”. (that’s why HDL has highest content of phospholipids!)

*LCAT : lecithin-cholesterol acyl transferase.

*PCAT: phosphatidylcholine-cholesterol acyl transferase. (PCAT=LCAT)

*Acyl= fatty acid.

PHOSPHOLIPASES

- What are they?

*A group of enzymes that catalyze the cleavage of phospholipids

*some phospholipases possess substrate specificity for certain phospholipid species so it has **remodeling** and **degradation** function.

For glycerophospholipids

- Phospholipases **A1**, **A2**, **C** and **D**.
- Where do they present? in **all tissues**, **pancreatic juice**, **snake venoms** and **bacterial toxins**.

Phospholipase A1:
break the bond of the carbon number 1 of glycerol (**C1**).

Phospholipase A2:
- break the bond of **C2**.
- the main enzyme in **remodeling** of phospholipids to make **Surfactant**.
-It's also can be found in pancreatic enzymes (help in digestion).

Phospholipase C:
- found in **liver lysosomes** and **bacterial toxin**, and activated by PIP system ,so it is plays a role in producing second messengers.

Phospholipase D :
can be found in **plant tissue**.

For sphingophospholipids

- Lysosomal phospholipase: **Sphingomyelinase**
Catalyze Sphingomyelin
to produce \longrightarrow Ceramide + Phosphocholine

FUNCTIONS OF PHOSPHOLIPASES

1- Degradation of phospholipids

Examples:

1. -Production of second messengers.
2. Digestion of phospholipids by pancreatic juice.
3. Pathogenic bacteria degrade phospholipids of membranes and **causing spread of infection**.

2- Remodelling of phospholipids

-what are they? Specific phospholipases that remove fatty acid from phospholipids.

-Examples:

A- Phospholipase A2 is important for the **remodelling** of phospholipids to produce the lung surfactant.

B- Replacement of fatty acid by alternative fatty acid using **fatty acyl CoA transferase**

e.g.,

- Binding of 2 palmitic acids in Dipalmitoylphosphatidylcholine (DPPC)
- Binding of arachidonic to carbon 2 of phosphatidylcholine.

Remodeling by the enzyme A2:

يكسر الانزيم الرابطة مع الفاتي اسيد على الكربونة الثانية، ويركب بالماتيك اسيد - احضرها له الترانسفيريز - على الكربونة، طبعا الكربونة الأولى عليها بالماتيك اسيد، فصار فيه اثنين بالماتيك اسيدز على كربونتين متجاورتين ، فيصبح اسم المركب:

Dipalmitoylphosphatidylcholine

PHOSPHOLIPASE A_2 Important:

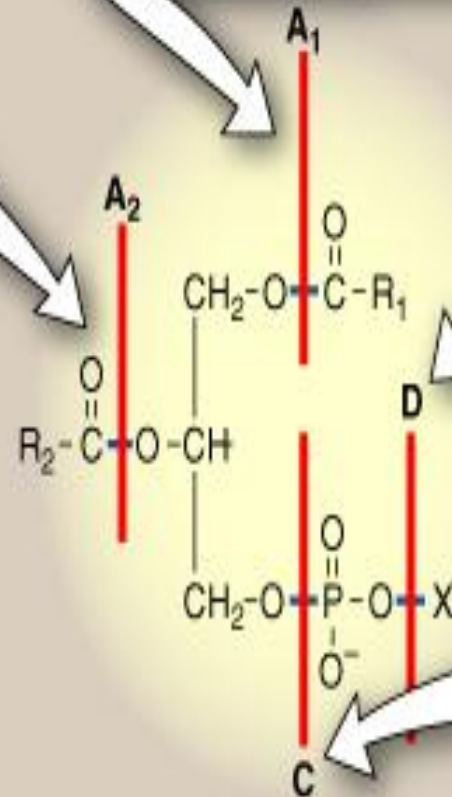
- *Phospholipase A_2* is present in many mammalian tissues and pancreatic juice. It is also present in snake and bee venoms.
- *Phospholipase A_2* , acting on phosphatidylinositol, releases arachidonic acid (the precursor of the prostaglandins).
- Pancreatic secretions are especially rich in the *phospholipase A_2* proenzyme, which is activated by *trypsin* and requires bile salts for activity.
- *Phospholipase A_2* is inhibited by glucocorticoids (for example, cortisol).

PHOSPHOLIPASE A_1

- *Phospholipase A_1* is present in many mammalian tissues.

PHOSPHOLIPASE D

- *Phospholipase D* is found primarily in plant tissue.



PHOSPHOLIPASE C

- *Phospholipase C* is found in liver lysosomes and the α -toxin of clostridia and other bacilli.
- Membrane-bound *phospholipase C* is activated by the PIP₂ system and, thus, plays a role in producing second messengers.

Ceramide: Parent Sphingolipid Compound

Ceramides are a family of waxy lipid molecules. A ceramide is composed of sphingosine and a fatty acid. Ceramides are found in high concentrations within the cell membrane of cells.

Structure and function of myelin sheath:

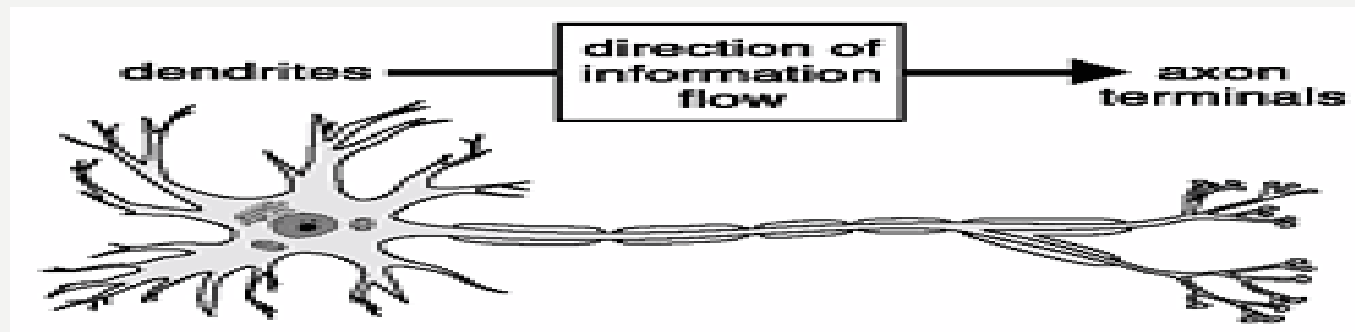
A-Myelin structure : Lipids 80% :

1- Glycolipids⁽¹⁾ (mainly)

2-Sphingomyelin

B- proteins 20%.

Myelin sheath insulates the nerve axon to avoid signal leakage and greatly speeds up the transmission of impulses along axons **Direction of nerve impulse**



(1):are lipids with a carbohydrate attached by a glycosidic bond. [1] Their role is to serve as markers for cellular recognition and also to provide energy. The carbohydrates are found on the outer surface of all eukaryotic cell membranes.

1-Lung surfactant is a function of :

- A. Membrane-bound phospholipids.
- B. IP3.
- C. DAG
- D. Non-membrane-bound phospholipids.

2-function of membrane-bound phospholipids:

- A. Detergent effect.
- B. Anchoring of proteins to membrane.
- C. Structural of lipoproteins.

3-Congenital RDS in neonatal issue to insufficient production of:

- A. Dipalmitoylecithin.
- B. Phosphatidylinositol.
- C. Lipoproteins.
- D. Phospholipases.

4-The phospholipid that is involved in signaling:

- A. Triacylglycerol.
- B. Lecithin.
- C. Phosphatidylinositol.
- D. Sphingomyelin.

5-The second messengers in phosphatidylinositol/calcium system are:

- A. IP3 & DAG
- B. HDL & VLDL
- C. cGMP & IP3
- D. IP3 & DAG

6-The class of lipoprotein that has highest content of phospholipids is:

- A. VLDL
- B. HDL
- C. LDL
- D. Chylomicrons.

7-The phospholipase that are mainly found in pancreatic enzymes is:

- A. A2
- B. A1
- C. C
- D. D

8-To prevent RDS , the mother must be given shortly before delivery :

- A. Intra-tracheal administration of surfactant .
- B. phospholipase C.
- C. Glucocorticoids.
- D. phosphatidylcholine.

SAQs

1) WHAT ARE THE FUNCTIONS OF PHOSPHOLIPIDS ?

Membrane bound phospholipids	Non -Membrane bound phospholipids
<ul style="list-style-type: none"> *Structural : predominant lipids of cell membrane * Anchoring : the proteins to membrane * Signaling : source of IP3 and DAG * Myelin sheath : speed up transmission of nerve impulses . 	<ul style="list-style-type: none"> • Lung surfactant : re-inflation of alveoli . • Detergent effect . • Structural : coat lipoprotein.

2) GIVE TOW NAMES OF SIMPLE AND COMPLEX LIPIDS ?

SIMPLE LIPIDS : 1- FATTY ACIDS 2- KETONE BODIES 3- CHOLESTEROL .

COMPLEX LIPIDS : 1- PHOSPHOLIPIDS 2- LIPOPROTEINS 3- GLYCOPROTEIN .

SAQS

3) WHAT ARE THE MAJOR EXAMPLES OF GLYCEROPHOSPHOLIPIDS ?

- 1- phosphatidylcholine (lecithin)
- 2- phosphatidylinositol.

4) TALK ABOUT CONGENITAL RESPIRATORY DISTRESS SYNDROME (RDS) ?

It is a disease that cause by insufficient production of lung surfactant (Lecithin) and it occur in pre-term babies . **Diagnosis by** lecithin/sphingomyeline ratio . Normal ratio 2 or above . **Prevention by** given glucocorticoids to the pregnant mother with low L/s . **Treatment by** intratracheal administration .

5) WHERE IS THE PLACE FOR SYNTHESIS AND SECRETION OF DIPALMITOYLECITHIN ?

It synthesis and secretion by granular pneumocytes .

6) TALK ABOUT PHOSPHOLIPASES ?

A phospholipase is an enzyme that hydrolyzes phospholipids into fatty acids and other lipophilic substances . It classification into :

- 1- for glycerophospholipids : phospholipases A1 , A2 , C and D .
- 2- for sphingophospholipids : lysosomal phospholipase (sphingomyelinase)

Team Members:

Team Leaders:

- شهد العنزي.
- عبدالله الغزي.

- نوره الرميح.
- بدور جليدان.
- أثير النشوان.
- علا النهير.
- أفنان المالكي.
- خوله العريني.
- دلال الحزيمي.
- رهنف بن عباد.
- منيره السلولي.
- غاده القصيمي.
- نوف الرشيد.
- مي العقيل.
- هديل الغرير.
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